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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,407	12/13/2001	Kevin P. Baker	P2830P1C61	8089

35489 7590 05/19/2005

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EXAMINER	
NICKOL, GARY B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 05/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,407	BAKER ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-35,38-40 and 44-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-35,38-40 and 44-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Baker *et al.*

Earliest date of priority: 02-18-2000

Response to Amendment

The Amendment filed 04-26-05 in response to the Office Action of 02-10-2005 is acknowledged and has been entered.

Claims 31-35, 38-40, 44-47 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Upon review and reconsideration, the following rejection has been re-instated.

Claims 31-35, 38-40, 44-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the

predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claimed invention is broadly drawn to isolated nucleic acids, including those comprising SEQ ID NO:305 and those encoding the polypeptide of SEQ ID NO:306. The specification appears to contemplate some type of diagnostic utility for the claimed invention according to the gene amplification studies as set forth on page 494. However, one of ordinary skill in the art would not know how to predictably use the claimed invention based on the guidance and teachings in the specification. In particular, the specification teaches that several primary lung tumors exhibited amplification of the PRO1558 gene. For example, see page 503, column 12. The ΔCt for HF-000840 and HF000842 was 1.39 and 1.24, respectively. This would appear to indicate an approximately 2 fold-amplification of PRO1558 *relative to normal* . However, the conditions which govern the "control" of the experiment appear to lend non-enablement to the results. In the instant case, the specification teaches that the negative control consisted of DNA isolated from the *blood* cells of ten normal healthy individuals (page 494, line 31; page 500, line 22). However, the specification is silent as to any correlation between DNA isolated from lung cancer and DNA isolated from the blood. How exactly is DNA isolated from the blood considered a control especially since it is not clear what type of blood cells were isolated? Furthermore, the specification is silent on whether or not PRO1558 is shed or secreted into the blood stream under normal and or cancerous conditions. Thus, applicants are attempting to compare the expression of PRO1558 in lung tumor specimens versus its expression in a non-related tissue. However, to those of ordinary skill in the art of oncology, a true negative control would more than likely comprise the analysis of the expression of PRO1558 in the

corresponding normal tissue, i.e. normal lung tissue, thus excluding the possibility of false-positive results. Many proteins, including PRO1558, are expressed in a variety of normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed sequence is present only in cancer tissue to the exclusion of the corresponding normal tissue.

Thus, based on the lack of guidance and exemplification in the specification, and in view of the state of the art, one of ordinary skill in the art would not be able to use the invention in a predictable manner. Thus, it would require undue experimentation to practice the invention as claimed.

Applicants appear to argue (Response, page 12, 11-12-2004) that the results speak for themselves. That is, because the specification clearly provides that the PR01558 gene was amplified in six of the lung tumors, then one of skill in the art would know exactly how to make and use the claimed invention. Applicants further argue that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. These arguments have been carefully considered but are not found persuasive as applicants have clearly not addressed the issues regarding the controlled conditions. Further, although experimentation may be complex, it is unclear if the relevant diagnostic art typically engages in such experimentation. For example, it would appear that applicants agreed with the Examiner's rationale regarding the controlled condition in stating that they "agree with the Examiner that comparing the expression of PRO1558 in lung tumor with the expression of PRO1558 in normal lung tissue" is a true negative control. On the other hand, applicants argue that the negative control as taught in the specification is also considered a "true negative control". However, applicants only reiterate the results (Brief, page 13) and offer no evidence to

support such an assertion. Thus, applicant's arguments have not been found persuasive, and the rejection is maintained.

New Rejection/Objections:

Claim 38 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 33. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper to object to the claims as being substantial duplicates. See MPEP § 706.03(k).

Claim 31, first line, is objected to for reciting "An isolated nucleic acid of encoding" which appears grammatically incorrect.

Claims 31-32, and 34-35 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising SEQ ID NO:35, does not reasonably provide enablement for isolated nucleic acids encoding polypeptides of SEQ ID NO:306. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or

guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. The claims are broadly drawn to isolated nucleic acids encoding polypeptides of SEQ ID NO:306 wherein the nucleic acid encoding the polypeptide is amplified in lung or colon tumors. Thus, the claims broadly encompass degenerate polynucleotides that encode polypeptide that diagnose lung or colon tumors. However, the increased copy number of DNA does not provide a readily apparent use for the polypeptide, for which there is no information regarding level of expression, activity, or role in cancer. Further, degenerate or variant polynucleotides do not necessarily predict protein expression. For example, Konopka *et al.* (Proc.Natl.Acad.Sci., Vol. 83, June 1986, pp. 4049-4052) teach the variable expression of the c-abl oncogene in B-cells derived from chronic myelogenous leukemia patients. Konopka *et al.* teach that protein expression is not related to amplification of the abl gene, but due to the variations in the level of mRNA (abstract). Further, it is well known in the art that the control of gene expression can occur at multiple stages and that production of RNA cannot inevitably be equated with production of protein. (Lewin, B. Genes VI, Oxford University Press, Inc., NY, Chapter 29, 1997). Thus, it would not be predictable that all degenerate nucleotide endcoding variant polypeptids with sequence similarity to the amino acids of SEQ ID NO:306 would be useful for diagnostic purposes, especially in analyzing gene amplification in tumors such as lung or colon tumors.

Thus, for the reasons set forth above, it appears that it would require undue experimentation to practice the invention as broadly claimed.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Primary Examiner
Art Unit 1642

GBN

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER